

## **Amendments to the Claims**

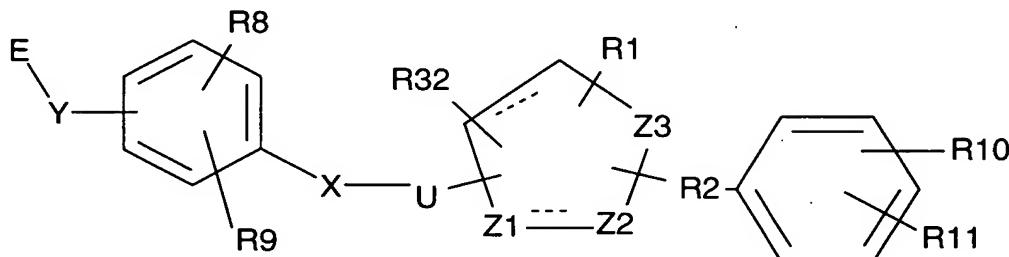
Please cancel claims: 4, 7, 40, 55, 60, 61, 62, 66, and 67

## **In the Claims**

This listing of claims will replace all prior versions and listings of claims in the application.

**What is claimed is:**

1. (Currently amended) A compound of the Formula I':



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

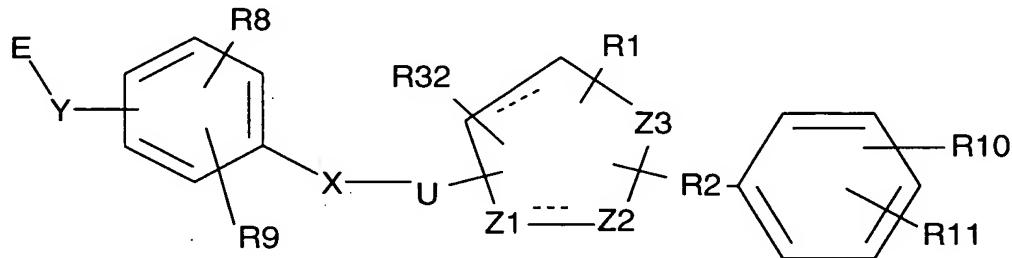
- (a) R1 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkenyl, aryl-C<sub>0</sub>-C<sub>4</sub>-alkyl, aryl-C<sub>1</sub>-C<sub>4</sub>-heteroalkyl, heteroaryl-C<sub>0</sub>-C<sub>4</sub>-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-C<sub>2</sub>-alkyl, and, wherein C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkenyl, aryl-C<sub>0</sub>-C<sub>4</sub>-alkyl, aryl-C<sub>1</sub>-C<sub>4</sub>-heteroalkyl, heteroaryl-C<sub>0</sub>-C<sub>4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-C<sub>2</sub>-alkyl are each optionally substituted with from one to three substituents independently selected from R1';
- (b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR<sub>12</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryloxy, aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl, heterocycloalkyl, C(O)R<sub>13</sub>, COOR<sub>14</sub>, OC(O)R<sub>15</sub>, OS(O)<sub>2</sub>R<sub>16</sub>, N(R<sub>17</sub>)<sub>2</sub>, NR<sub>18</sub>C(O)R<sub>19</sub>, NR<sub>20</sub>SO<sub>2</sub>R<sub>21</sub>, SR<sub>22</sub>, S(O)R<sub>23</sub>, S(O)<sub>2</sub>R<sub>24</sub>, and S(O)<sub>2</sub>N(R<sub>25</sub>)<sub>2</sub>; R<sub>12</sub>, R<sub>13</sub>, R<sub>14</sub>, R<sub>15</sub>, R<sub>16</sub>, R<sub>17</sub>, R<sub>18</sub>, R<sub>19</sub>, R<sub>20</sub>, R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, R<sub>24</sub> and R<sub>25</sub> are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl;
- (c) R<sub>2</sub> is selected from the group consisting of C<sub>0</sub>-C<sub>8</sub> alkyl and C<sub>1</sub>-C<sub>4</sub>-heteroalkyl;
- (d) X is selected from the group consisting of a single bond, O, S, S(O)<sub>2</sub> and N;

- (e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with from one to four substituents each independently selected from R30;
- (f) Y is selected from the group consisting of C, NH, and a single bond;
- (g) E is C(R3)(R4)A or A and wherein
  - (i) A is selected from the group consisting of carboxyl, tetrazole, C<sub>1</sub>-C<sub>6</sub> alkynitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R<sup>7</sup>;
  - (ii) each R<sup>7</sup> is independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl C<sub>0</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl;
  - (iii) R3 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>5</sub> alkyl, and C<sub>1</sub>-C<sub>5</sub> alkoxy; and
  - (iv) R4 is selected from the group consisting of H, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl C<sub>0</sub>-C<sub>4</sub> alkyl, and R3 and R4 are optionally combined to form a C<sub>3</sub>-C<sub>4</sub> cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with from one to three substituents each independently selected from R26;
- (h) Z1 and Z2 are each independently selected from the group consisting of N, O, and C with the proviso that at least one of Z1 and Z2 is N;
- (i) Z3 is selected from the group consisting of N, O, and C;
- (j) R8 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, and halo;
- (k) R9 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, halo, aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl, C<sub>1</sub>-C<sub>6</sub> allyl, and OR29, and wherein aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;
- (l) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12'', C<sub>0</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0</sub>-C<sub>4</sub>-alkyl, aryl-C<sub>1</sub>-C<sub>4</sub>-heteroalkyl, heteroaryl-C<sub>0</sub>-C<sub>4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-C<sub>2</sub>-alkyl, aryloxy,

C(O)R13', COOR14', OC(O)R15', OS(O)<sub>2</sub>R16', N(R17')<sub>2</sub>, NR18'C(O)R19', NR20'SO<sub>2</sub>R21', SR22', S(O)R23', S(O)<sub>2</sub>R24', and S(O)<sub>2</sub>N(R25')<sub>2</sub>; and wherein aryl-C<sub>0</sub>-4-alkyl, aryl-C<sub>1</sub>-4-heteroalkyl, heteroaryl-C<sub>0</sub>-4-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl are each optionally substituted with from one to three independently selected from R28;

- (m) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl;
- (n) R30 is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, aryl-C<sub>0</sub>-4-alkyl, aryl-C<sub>1</sub>-4-heteroalkyl, heteroaryl-C<sub>0</sub>-4-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl, and wherein C<sub>1</sub>-C<sub>6</sub> alkyl, aryl-C<sub>0</sub>-4-alkyl, aryl-C<sub>1</sub>-4-heteroalkyl, heteroaryl-C<sub>0</sub>-4-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;
- (o) R32 is selected from the group consisting of a bond, hydrogen, halo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, and C<sub>1</sub>-C<sub>6</sub> alkyloxo; and
- (p) ---- is optionally a bond to form a double bond at the indicated position.

2. (Currently amended) A compound of the Formula I'':



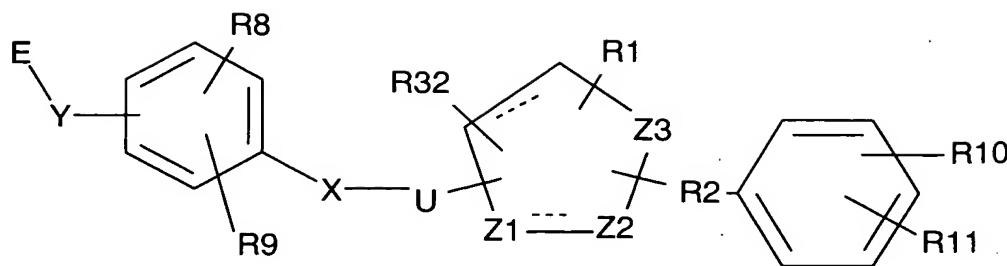
and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

- (a) R1 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkenyl, aryl-C<sub>0</sub>-4-alkyl, aryl-C<sub>1</sub>-4-heteroalkyl, heteroaryl-C<sub>0</sub>-4-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl, and, wherein C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkenyl, aryl-C<sub>0</sub>-4-alkyl, aryl-C<sub>1</sub>-4-heteroalkyl, heteroaryl-C<sub>0</sub>-4-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl are each optionally substituted with from one to three substituents independently selected from R1';

- (b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryloxy, aryl-C<sub>0</sub>-4-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, OS(O)<sub>2</sub>R16, N(R17)<sub>2</sub>, NR18C(O)R19, NR20SO<sub>2</sub>R21, SR22, S(O)R23, S(O)<sub>2</sub>R24, and S(O)<sub>2</sub>N(R25)<sub>2</sub>; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl;
- (c) R2 is selected from the group consisting of C<sub>0</sub>-C<sub>8</sub> alkyl and C<sub>1</sub>-4-heteroalkyl;
- (d) X is selected from the group consisting of a single bond, O, S, S(O)<sub>2</sub> and N;
- (e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is substituted with from one to four substituents each independently selected from R30;
- (f) Y is selected from the group consisting of C, and O, S, NH and a single bond;
- (g) E is C(R3)(R4)A or A and wherein
  - (i) A is selected from the group consisting of carboxyl, tetrazole, C<sub>1</sub>-C<sub>6</sub> alkynitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R<sup>7</sup>;
  - (ii) each R<sup>7</sup> is independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl C<sub>0</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl;
  - (iii) R3 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>5</sub> alkyl, and C<sub>1</sub>-C<sub>5</sub> alkoxy; and
  - (iv) R4 is selected from the group consisting of H, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl C<sub>0</sub>-C<sub>4</sub> alkyl, and R3 and R4 are optionally combined to form a C<sub>3</sub>-C<sub>4</sub> cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with from one to three substituents each independently selected from R26;
- (h) Z1 and Z2 are each independently selected from the group consisting of N, O, and C with the proviso that at least one of Z1 and Z2 is N;
- (i) Z3 is selected from the group consisting of N, O, and C;

- (j) R8 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, and halo;
- (k) R9 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, halo, aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl, C<sub>1</sub>-C<sub>6</sub> allyl, and OR29, and wherein aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;
- (l) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12'', C<sub>0</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0</sub>-4-alkyl, aryl- C<sub>1</sub>-4-heteroalkyl, heteroaryl-C<sub>0</sub>-4-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', OS(O)<sub>2</sub>R16', N(R17')<sub>2</sub>, NR18'C(O)R19', NR20'SO<sub>2</sub>R21', SR22', S(O)R23', S(O)<sub>2</sub>R24', and S(O)<sub>2</sub>N(R25')<sub>2</sub>; and wherein aryl-C<sub>0</sub>-4-alkyl, aryl- C<sub>1</sub>-4-heteroalkyl, heteroaryl-C<sub>0</sub>-4-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl are each optionally substituted with from one to three independently selected from R28;
- (m) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl;
- (n) R30 is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, aryl-C<sub>0</sub>-4-alkyl, aryl- C<sub>1</sub>-4-heteroalkyl, heteroaryl-C<sub>0</sub>-4-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl, and wherein C<sub>1</sub>-C<sub>6</sub> alkyl, aryl-C<sub>0</sub>-4-alkyl, aryl- C<sub>1</sub>-4-heteroalkyl, heteroaryl-C<sub>0</sub>-4-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;
- (o) R32 is selected from the group consisting of a bond, hydrogen, halo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, and C<sub>1</sub>-C<sub>6</sub> alkyloxo; and
- (p) ---- is optionally a bond to form a double bond at the indicated position.

3. (Currently amended) A compound as claimed by Claim 2 of the Formula I'':



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

- (a) R1 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkenyl, aryl-C<sub>0</sub>-4-alkyl, aryl-C<sub>1</sub>-4-heteroalkyl, heteroaryl-C<sub>0</sub>-4-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl, and, wherein C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkenyl, aryl-C<sub>0</sub>-4-alkyl, aryl-C<sub>1</sub>-4-heteroalkyl, heteroaryl-C<sub>0</sub>-4-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl are each optionally substituted with from one to three substituents independently selected from R1';
- (b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryloxy, aryl-C<sub>0</sub>-4-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, OS(O)<sub>2</sub>R16, N(R17)<sub>2</sub>, NR18C(O)R19, NR20SO<sub>2</sub>R21, SR22, S(O)R23, S(O)<sub>2</sub>R24, and S(O)<sub>2</sub>N(R25)<sub>2</sub>; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl;
- (c) R2 is selected from the group consisting of C<sub>0</sub>-C<sub>8</sub> alkyl and C<sub>1</sub>-4-heteroalkyl;
- (d) X is selected from the group consisting of a single bond, O, S, S(O)<sub>2</sub> and N;
- (e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with from one to four substituents each independently selected from R30;
- (f) Y is selected from the group consisting of O, S, and C, NH and a single bond;
- (g) E is C(R3)(R4)A; wherein
  - (i) A is selected from the group consisting of carboxyl, tetrazole, C<sub>1</sub>-C<sub>6</sub> alkylnitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide,

acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R<sup>7</sup>;

(ii) each R<sup>7</sup> is independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl C<sub>0</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl;

(iii) R<sub>3</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkyl, and C<sub>1</sub>-C<sub>5</sub> alkoxy; and

(iv) R<sub>4</sub> is selected from the group consisting of H, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl C<sub>0</sub>-C<sub>4</sub> alkyl, and R<sub>3</sub> and R<sub>4</sub> are optionally combined to form a C<sub>3</sub>-C<sub>4</sub> cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with from one to three substituents each independently selected from R<sub>26</sub>;

with the proviso that when Y is O then R<sub>4</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl C<sub>0</sub>-C<sub>4</sub> alkyl, and R<sub>3</sub> and R<sub>4</sub> are optionally combined to form a C<sub>3</sub>-C<sub>4</sub> cycloalkyl, and wherein alkyl, alkoxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three each independently selected from R<sub>26</sub>;

(h) Z<sub>1</sub> and Z<sub>2</sub> are each independently selected from the group consisting of N, O, and C with the proviso that at least one of Z<sub>1</sub> and Z<sub>2</sub> is N;

(i) Z<sub>3</sub> is selected from the group consisting of N, O, and C;

(j) R<sub>8</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, and halo;

(k) R<sub>9</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkylenyl, halo, aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl, C<sub>1</sub>-C<sub>6</sub> allyl, and OR<sub>29</sub>, and wherein aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R<sub>27</sub>; R<sub>29</sub> is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;

(l) R<sub>10</sub>, R<sub>11</sub> are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR<sub>12''</sub>, C<sub>0</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0</sub>-C<sub>4</sub>-alkyl, aryl-C<sub>1</sub>-C<sub>4</sub>-heteroalkyl, heteroaryl-C<sub>0</sub>-C<sub>4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-C<sub>2</sub>-alkyl, aryloxy, C(O)R<sub>13'</sub>, COOR<sub>14'</sub>, OC(O)R<sub>15'</sub>, OS(O)<sub>2</sub>R<sub>16'</sub>, N(R<sub>17'</sub>)<sub>2</sub>, NR<sub>18'</sub>C(O)R<sub>19'</sub>, NR<sub>20'</sub>SO<sub>2</sub>R<sub>21'</sub>, SR<sub>22'</sub>, S(O)R<sub>23'</sub>, S(O)<sub>2</sub>R<sub>24'</sub>, and S(O)<sub>2</sub>N(R<sub>25'</sub>)<sub>2</sub>; and wherein aryl-

$C_{0-4}$ -alkyl, aryl-  $C_{1-4}$ -heteroalkyl, heteroaryl- $C_{0-4}$ -alkyl, and  $C_3-C_6$  cycloalkylaryl- $C_{0-2}$ -alkyl are each optionally substituted with from one to three independently selected from R28;

- (m)  $R_{12}', R_{12}'', R_{13}', R_{14}', R_{15}', R_{16}', R_{17}', R_{18}', R_{19}', R_{20}', R_{21}', R_{22}', R_{23}', R_{24}',$  and  $R_{25}'$  are each independently selected from the group consisting of hydrogen,  $C_1-C_6$  alkyl and aryl;
- (n)  $R_{30}$  is selected from the group consisting of  $C_1-C_6$  alkyl, aryl- $C_{0-4}$ -alkyl, aryl-  $C_{1-4}$ -heteroalkyl, heteroaryl- $C_{0-4}$ -alkyl, and  $C_3-C_6$  cycloalkylaryl- $C_{0-2}$ -alkyl, and wherein  $C_1-C_6$  alkyl, aryl- $C_{0-4}$ -alkyl, aryl-  $C_{1-4}$ -heteroalkyl, heteroaryl- $C_{0-4}$ -alkyl, and  $C_3-C_6$  cycloalkylaryl- $C_{0-2}$ -alkyl are each optionally substituted with from one to three substituents each independently selected from R31;
- (o)  $R_{32}$  is selected from the group consisting of a bond, hydrogen, halo,  $C_1-C_6$  alkyl,  $C_1-C_6$  haloalkyl, and  $C_1-C_6$  alkyloxo; and
- (p) ---- is optionally a bond to form a double bond at the indicated position.

4. (Canceled)

5. (Currently amended) A compound as claimed by any one of Claims 1 ~~through 4 or 2~~ wherein X is -O-.

6. (Currently amended) A compound as claimed by any one of Claims 1 ~~through 4 or 2~~ wherein X is -S-.

7. (Canceled)

8. (Currently amended) A compound as claimed by ~~any one of~~ Claims 2 ~~through 6~~ wherein Y is C.

9. (Currently amended) A compound as claimed by ~~any one of~~ Claims 1 ~~through 6 or 2~~ wherein Y is S.

10. (Currently amended) A compound as claimed by any one of Claims 1 ~~through 9 or 2~~ wherein Z3 is N.

11. (Currently amended) A compound as claimed by any one of Claims 1 ~~or 2 through 9~~ wherein Z3 is O.

12. (Currently amended) A compound as claimed by any one of Claims 1 ~~or 2 through 11~~ wherein Z2 is N.

13. (Currently amended) A compound as claimed by any one of Claims 1, or 2 through 12 wherein Z1 is C.
14. (Currently amended) A compound as claimed by any one of Claims 1 or 2 through 12 wherein Z1 is N.
15. (Currently amended) A compound as claimed by any one of Claims 1 or 2 through 12 wherein Z1 is O.
16. (Currently amended) A compound as claimed by any one of Claims 1 or 2 through 15 wherein ---- is a bond to form a double bond at the designated location on Formula I.
17. (Currently amended) A compound as claimed by any one of Claims 1 through 16\_14 wherein E is C(R3)(R4)A.
18. (Currently amended) A compound as claimed by any one of Claims 1 or 2 through 17 wherein A is COOH.
19. (Currently amended) A compound as claimed by any one of Claims 1 through 18 wherein R10 is haloalkyl.
20. (Currently amended) A compound as claimed by any one of Claims 1 through 18 wherein R10 is CF<sub>3</sub>.
21. (Currently amended) A compound as claimed by any one of Claims 1 through 18 wherein R10 is haloalkyloxy.
22. (Currently amended) A compound as claimed by any one of Claims 1 through 18 wherein R10 and R11 are each independently selected from the group consisting of hydrogen, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12'', C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, and C<sub>1</sub>-C<sub>6</sub> haloalkyloxy.
23. (Currently amended) A compound as claimed by any one of Claims 1 through 18 wherein R10 is selected from the group consisting of C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0-4</sub>-alkyl, aryl-C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl, and aryloxy.
24. (Currently amended) A compound as claimed by any one of Claims 1\_2 through 23 wherein R1 is optionally substituted C<sub>2</sub>-C<sub>3</sub> arylalkyl.
25. (Currently amended) A compound as claimed by any one of Claims 1 through 23\_18, wherein R8 and R9 are each independently selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>3</sub> alkyl.

26. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 23 and 25~~ 18 wherein R1, R2, R3, and R4 are each independently selected from the group consisting of C<sub>1</sub>-C<sub>2</sub> alkyl.
27. (Currently amended) A compound as claimed by ~~any one of Claims 1 through Claim 23 and 25~~ 18 wherein R1, R3, and R4 are each independently selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>2</sub> alkyl.
28. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 25 or Claim 27~~ 18 wherein R2 is a bond.
29. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 25 or 28~~ 18 wherein U is C<sub>1</sub>-C<sub>3</sub> alkyl.
30. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 29~~ wherein U is saturated.
31. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 30~~ 18 wherein U is substituted with C<sub>1</sub>-C<sub>3</sub> alkyl.
32. (Currently amended) A compound as claimed by ~~any one of Claims 29, 30 and 31~~ wherein one carbon of the aliphatic linker is replaced with an O.
33. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 31~~ 18 wherein U is an aliphatic linker having one carbon replaced by S.
34. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 33~~ 18 wherein the aliphatic linker is substituted with from one to three substituents each independently selected from R30.
35. (Original) A compound as claimed by Claim 34 wherein the aliphatic linker is substituted with from one to two substituents each independently selected from R30.
36. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 35~~ 18 wherein each R30 is independently selected from the group consisting of C1-C6 alkyl.
37. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 36~~ wherein each R30 is independently selected from the group consisting of C2-C3 alkyl.
38. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 37~~ 34 wherein R30 is selected from the group consisting of aryl-C<sub>0-4</sub>-alkyl, aryl- C<sub>1-4</sub>-heteroalkyl, heteroaryl-C<sub>0-4</sub>-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0-2</sub>-alkyl.

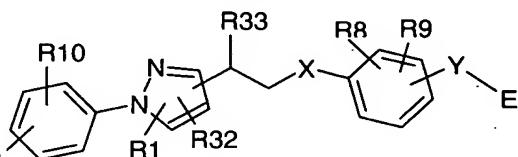
39. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 38~~ 18 wherein “---“ each form a double bond in the five membered ring, Z2 and Z3 are each N and Z3 is bonded to R2.

40. (Canceled)

41. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 40~~ 36 wherein U is substituted with methyl.

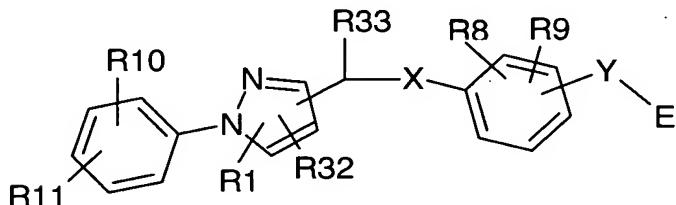
42. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 41~~ 29 wherein U is methylene.

43. (Currently amended) A compound as claimed by any one of ~~Claims 1 or 2 through 10, one of Claims 17 through 25, or one of Claims 27 through 35~~ represented by the



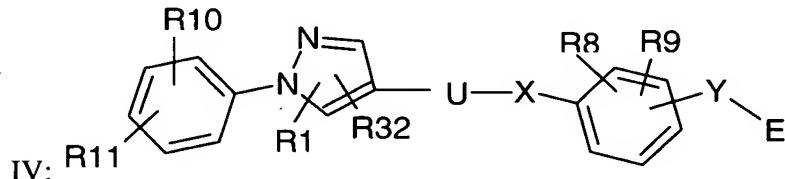
following Structural Formula II: R11  
wherein R33 is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>3</sub> alkyl.

44. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 10, or one of Claims 17 through 36~~ 18 represented by the following Structural Formula III:

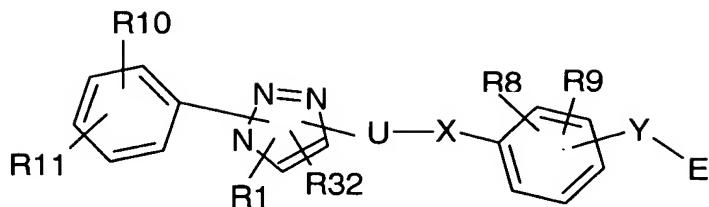


wherein R33 is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>3</sub> alkyl.

45. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 10, or one of Claims 17 through 42~~ 18 represented by the following Structural Formula



46. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 10, or one of Claims 17 through 42~~ 18 represented by the following Structural Formula V:



47. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 46~~ 18 wherein X and Y are substituted at a 1,4-position, such that X and Y are para substituted to one another.

48. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 46~~ 18 wherein X and Y are substituted at a 1,3-position, such that X and Y are meta substituted to one another.

49. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 4~~ 18 wherein the compound is selected from the group consisting of  
 (3-{1-[3-Methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-phenyl)-acetic acid;  
 (3-{1-[3-Methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-ethoxy}-phenyl)-acetic acid;  
 (4-{1-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-2-methyl-phenoxy)-acetic acid;  
 3-(4-{1-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-2-methyl-phenyl)-propionic acid;  
 3-{4-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethylsulfanyl]-2-methyl-phenyl}-propionic acid;  
 {4-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethylsulfanyl]-2-methyl-phenoxy}-acetic acid;  
 {4-[5-Chloro-3-isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethylsulfanyl]-2-methyl-phenoxy}-acetic acid;  
 3-{4-[5-Chloro-3-isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethylsulfanyl]-2-methyl-phenyl}-propionic acid;  
 {3-[5-Chloro-3-isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethoxy]-phenyl}-acetic acid;

3-{4-[5-Chloro-3-isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethoxy]-2-methyl-phenyl}-propionic acid;

(S)-3-{4-[5-Chloro-3-isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethoxy]-phenyl}-2-methoxy-propionic acid;

{3-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethoxy]-phenyl}-acetic acid;

3-{4-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethoxy]-2-methyl-phenyl}-propionic acid;

3-{4-[3-Isopropyl-1-(4-trifluoromethoxy-phenyl)-1H-pyrazol-4-ylmethoxy]-phenyl}-2-methoxy-propionic acid;

3-[2-Methyl-4-(3-methyl-1-phenyl-1H-pyrazol-4-ylmethoxy)-phenyl]-propionic acid;

{2-Methyl-4-[5-methyl-1-(4-trifluoromethyl-phenyl)-1H-[1,2,3]triazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

3-{2-Methyl-4-[4-methyl-3-(4-trifluoromethyl-phenyl)-isoxazol-5-ylmethoxy]-phenyl}-propionic acid;

{4-[5-Isopropyl-2-(4-trifluoromethyl-phenyl)-3H-imidazol-4-ylmethylsulfanyl]-2-methyl-phenoxy}-acetic acid; {4-[5-Isopropyl-3-methyl-2-(4-trifluoromethyl-phenyl)-3H-imidazol-4-ylmethylsulfanyl]-2-methyl-phenoxy}-acetic acid;

{4-[5-Isopropyl-3-methyl-2-(4-trifluoromethyl-phenyl)-3H-imidazol-4-ylmethoxy]-2-methyl-phenoxy}-acetic acid; and

3-{4-[5-Isopropyl-3-methyl-2-(4-trifluoromethyl-phenyl)-3H-imidazol-4-ylmethoxy]-2-methyl-phenyl}-propionic acid.

50. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 4~~ 18 which is a compound of Formula I selected from the group consisting of (R)-(2-Methyl-4-{1-[3-methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-phenoxy)-acetic acid, (S)-(2-Methyl-4-{1-[3-methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-phenoxy)-acetic acid, (R,S)-(2-Methyl-4-{1-[3-methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-propylsulfanyl}-phenoxy)-acetic acid, and (R,S)-(2-Methyl-4-{1-[3-methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-phenoxy)-acetic acid.

51. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 4~~ which is (R,S)-(2-Methyl-4-{1-[3-methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-ethylsulfanyl}-phenoxy)-acetic acid.
52. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 50\_2~~ that is the S conformation.
53. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 50\_2~~ that is the R conformation.
54. (Currently amended) A pharmaceutical composition, comprising as an active ingredient, at least one compound as claimed by ~~any one of Claims 1 through 53\_18~~ together with a pharmaceutically acceptable carrier or diluent.
55. (Canceled)
56. (Currently amended) A method of treating diabetes mellitus in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of ~~Claims 1 through 53\_18~~.
57. (Currently amended) A method of treating metabolic disorder in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of ~~Claims 1 through 53\_18~~.
58. (Original) A method of Claim 57 wherein the mammal in need thereof is diagnosed as suffering from metabolic disorder.
59. (Currently amended) A method of selectively modulating a PPAR delta receptor comprising administering a compound as claimed by ~~any one of Claims 1 through 53\_2~~ to a mammal in need thereof.
60. (Canceled)
61. (Canceled)
62. (Canceled)
63. (Currently amended) A method for treating or preventing the progression of cardiovascular disease in a mammal in need thereof comprising administering a therapeutically effective amount of a compound as Claimed by ~~any one of Claims 1 through 53\_18~~.
64. (Original) A method as claimed by Claim 63 wherein the mammal is diagnosed as being in need of such treatment.

65. (Currently amended) A compound as claimed by ~~any one of Claims 1 through 53~~ 18 wherein the compound is radiolabeled.
66. (Canceled)
67. (Canceled)